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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 5 : A61K 7/24 — A1

(11) International Publication Number: WO 94/03147

(43) International Publication Date: 17 February 1994 (17.02.94)

(21) International Application Number: PCT/US93/06744

(22) International Filing Date: 19 July 1993 (19.07.93)

(30) Priority data:
07/923,037 31 July 1992 (31.07.92) US

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(81) Designated States: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KP, KR, KZ, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(54) Title: ORAL COMPOSITIONS

(57) Abstract

Oral compositions possessing antiplaque and antigingivitis properties containing stannous gluconate are described herein.

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ORAL COMPOSITIONS

TECHNICAL FIELD

The present invention relates to oral compositions such as liquid dentifrices, toothpastes, mouthwashes, chewing gum, tablets and powders which provide antiplaque and antigingivitis benefits.

BACKGROUND OF THE INVENTION

Plaque is recognized as a precursor of such oral diseases as caries and gingivitis. The gums of the mouth of humans and lower animals may be harmed by deposits of dental plaque, a combination of minerals and bacteria found in the mouth. The bacteria associated with plaque can secrete enzymes and endotoxins which can irritate the gums and cause an inflammatory gingivitis. As the gums become increasingly irritated by this process they have a tendency to bleed, lose their toughness and resiliency, and separate from the teeth, leaving periodontal pockets in which debris, secretions, more bacteria and toxins further accumulate. It is also possible for food to accumulate in these pockets, thereby providing nourishment for increased growth of bacteria and production of endotoxins and destructive enzymes. This can result in destruction of bone and gum tissue.

With such problems being possible from plaque/gingivitis it is not surprising that extensive efforts have been expended in trying to find effective treatment compositions. Many of these efforts have used quaternary ammonium compounds or bis-biquanides such as chlorhexidine which is used in Peridex® sold by The Procter & Gamble Company.

Another material which has been considered is stannous ion. Such a material is disclosed in Svatun B., "Plaque Inhibiting Effect of Dentifrices Containing Stannous Fluoride", Acta Odontol. Scand., 36, 205-210 (1978); and Bay I., and Rolla, G., "Plaque Inhibition and Improved Gingival Condition by Use of a Stannous Fluoride Toothpaste", Scand. J. Dent. Res., 88, 313-315 (1980). Additionally stannous fluoride stabilized with stannous gluconate has been used to treat plaque and gingivitis and disclosed in U.S. Patent 5,004,597, April 2,

1991 to Majeti et al.

In spite of the many disclosures in the antiplaque/antigingivitis area, the need for products still exists. The present invention is directed to the recognition that stannous gluconate when used without stannous fluoride, or with only very low levels of this material can provide plaque and gingivitis reductions.

It is an object of the present invention therefore to provide compositions which deliver an improved antiplaque/antigingivitis benefit.

It is a further object of the present invention to provide improved products utilizing stannous gluconate.

It is still a further object of the present invention to provide an effective method for treating plaque/gingivitis with the above described compositions.

These and other objects will become clearer from the detailed description which follows.

All percentages and ratios used herein are by weight of the total composition unless otherwise specified. Additionally, all measurements are made at 25°C in the composition or in an aqueous solution/dispersion unless otherwise specified.

SUMMARY OF THE INVENTION

The present invention embraces an oral composition comprising:

a) a safe and effective amount of stannous gluconate; and

b) a pharmaceutically acceptable carrier

wherein said composition has a pH of from about 3.0 to about 5.0 and is substantially free of calcium ion sources and stannous fluoride. By "substantially free" is meant less than about 0.05% for stannous fluoride and less than about 2.0% for the other materials.

The present invention also encompasses a method for retarding the development of plaque/gingivitis using these compositions.

DETAILED DESCRIPTION OF THE INVENTION

The compositions of the present invention comprise stannous gluconate and a pharmaceutically acceptable carrier.

By "oral composition" as used herein means a product which in the ordinary course of usage is not intentionally swallowed for purposes of systemic administration of particular therapeutic agents, but is rather retained in the oral cavity for a time sufficient to contact

substantially all of the dental surfaces and/or oral tissues for purposes of oral activity.

By "safe and effective amount" as used herein means sufficient amount of material to provide the desired benefit while being safe to the hard and soft tissues of the oral cavity.

By the term "comprising", as used herein, is meant that various additional components can be conjointly employed in the compositions of this invention as long as the listed materials perform their intended functions.

By the term "carrier", as used herein, is meant a suitable vehicle which is pharmaceutically acceptable and can be used to apply the present compositions in the oral cavity.

Stannous Gluconate

Stannous gluconate is the essential component of the present compositions. This material is a known stannous chelate and may be provided to the present compositions as the chelate or as separate soluble stannous and gluconate salts and the chelate formed in-situ. Such salts include stannous chloride and sodium gluconate. Stannous gluconate is present in the present compositions at a level of from about 0.1% to about 11%, preferably from about 2% to about 4%.

Pharmaceutically Acceptable Carrier

The carrier for the stannous components can be any vehicle suitable for use in the oral cavity. Such carriers include the usual components of toothpastes, mouthwashes, tooth powders, prophylaxis pastes, lozenges, gums and the like and are more fully described hereinafter. Dentifrices and mouthwashes are the preferred systems.

The abrasive polishing material contemplated for use in the dentifrice aspect of the present invention can be any material which does not excessively abrade dentin. These include, for example, silicas including gels and precipitates, insoluble sodium polymetaphosphate, β-phase calcium pyrophosphate, hydrated alumina, and resinous abrasive materials such as particulate condensation products of urea and formaldehyde, and others such as disclosed by Cooley et al. in U.S. Patent 3,070,510, December 25, 1962, incorporated herein by reference. Mixtures of abrasives may also be used.

Silica dental abrasives, of various types, can provide the unique

the oral cavity safe and effective amounts of the compositions described herein. These amounts (e.g. from about 0.3 to about 15g), if it is a toothpaste or mouthwash, are kept in the mouth for from about 15 to about 60 seconds.

The following examples further describe and demonstrate preferred embodiments within the scope of the present invention. The examples are given solely for illustration and are not to be construed as limitations of this invention as many variations thereof are possible without departing from the spirit and scope thereof.

EXAMPLE I
Toothpaste

	Weight %	Weight %
Water	12.500	12.500
Sorbitol	45.425	44.552
Glycerin	10.198	10.198
Titanium Dioxide	0.525	0.525
Silica	20.000	20.000
Na Carboxymethyl Cellulose	1.050	1.050
Magnesium Aluminum Silicate	0.408	0.408
Na Alkyl Sulfate (27.9% Solution)	4.000	4.000
Na Gluconate	1.738	3.476
Stannous Chloride Dihydrate	1.794	1.794
Na Saccharin	0.200	0.200
Flavor	0.851	0.851
FD&C Blue #1 (1% Solution)	0.051	0.051
Na Monofluoro Phosphate	0.760	-
Na Hydroxide (50% Solution)	0.500	0.395
pH	4.5	4.5

EXAMPLE II
Mouthrinse

	Weight %	Weight %
Stannous Chloride Dihydrate	0.519	0.519
Sodium Gluconate	0.521	1.041
Glycerin	8.000	12.000
Sorbitol (70% Aqueous Solution)	-	-
Ethanol	10.000	10.000
Polysorbate 80	0.300	0.300
Sodium Saccharin	0.050	0.050
Flavor	0.150	0.150
Sodium Hydroxide	0.020	0.020
Benzoic Acid	0.050	0.050
FD&C Blue #1 (1% Solution)	0.020	0.020
Sodium Monofluoro Phosphate	0.183	-
Water pH	80.187	77.850

EXAMPLE III
Topical Gel

	Weight %	Weight %
Stannous Chloride Dihydrate	1.794	2.153
Sodium Gluconate	1.750	2.082

Glycerin	91.896	70.000
Sorbitol (70% Solution)	-	21.765
Sodium Carboxymethyl Cellulose	0.600	0.800
Hydroxyethyl Cellulose	-	-
Flavor	1.000	1.000
Sodium Saccharin	0.200	0.200
Sodium Alkyl Sulfate (27.9%)	2.000	2.000
Sodium Monofluoro Phosphate	0.760	-

EXAMPLE IV
Mouthrinse Tablet

Stannous Chloride Dihydrate	0.519g	0.519g
Sodium Gluconate	0.500g	0.700g
Flavor	0.150g	0.150g
Sodium Saccharin	0.050g	0.200g
Mannitol	0.773g	-
Sodium Carboxymethyl Cellulose	0.050g	-
Sodium Benzoate	0.030g	0.025g
Citric Acid	-	0.200g
Sodium Carbonate	-	0.100g
Sodium Bicarbonate	-	0.200g
Glycine	-	0.050g
Sodium Monofluoro Phosphate	0.183g	-
	2.255g	2.144g
	Dissolve in 97.745g water	Dissolve in 97.856g water

WHAT IS CLAIMED IS:

1. An oral composition effective in treating plaque/gingivitis comprising:
(a) a safe and effective amount of stannous gluconate; and
(b) a pharmaceutically acceptable carrier
wherein the ph of said composition is from about 3.0 to about 5.0 and said composition is substantially free of a calcium ion source(s) and stannous fluoride.

2. An oral composition according to Claim 1 wherein the amount of stannous gluconate is from about 0.1% to about 11%.

3. An oral composition according to Claim 1 or 2 wherein the pharmaceutically acceptable carrier is a toothpaste which also contains an effective amount of sodium monofluorophosphate.

4. An oral composition according to any of Claims 1-3 which also contains a silica dental abrasive.

5. An oral composition according to any of Claims 1-4 which also contains another stannous salt.

6. An oral composition according to Claim 2 wherein the pharmaceutically acceptable carrier is a mouthwash.

7. An oral composition according to Claim 6 which also contains a material selected from the group consisting of a humectant, ethanol, a nonionic surfactant and mixtures thereof.

8. An oral composition according to Claim 2 wherein the pharmaceutically acceptable carrier is a lozenge.

9. An oral composition according to Claim 2 wherein the pharmaceutically acceptable carrier is a chewing gum.

10. An oral composition according to Claim 2 which is in the form of a gel or a tablet.

INTERNATIONAL SEARCH REPORT

International Application No PCT/US 93/06744

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all)[6]

According to International Patent Classification (IPC) or to both National Classification and IPC

Int.Cl. 5 A61K7/24

II. FIELDS SEARCHED

Minimum Documentation Searched[7]

Classification System	Classification Symbols
Int.Cl. 5	A61K

Documentation Searched other than Minimum Documentation to the Extent that such Documents are included in the Fields Searched[8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT[9]

Category [10]	Citation of Document, [11] with indication, where appropriate, of the relevant passages [12]	Relevant to Claim No.[13]
Y	GB,A,1 009 480 (PROCTER & GAMBLE) 10 November 1965 see claims 1-12; example IA	1-10
Y	FR,A,2 406 437 (LION) 18 May 1979 see claims 1-6; example 2	1-10
Y	GB,A,2 216 005 (PROCTER & GAMBLE) 4 October 1989 see claims 1-11	1-10

[10] Special categories of cited documents :

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IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
12 OCTOBER 1993	1
International Searching Authority	**Signature of Authorized Officer**
EUROPEAN PATENT OFFICE	WILLEKENS

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO.

US 9306744
SA 77134

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 12/10/93
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